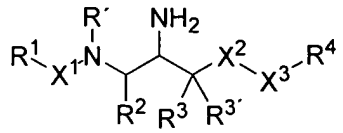
CLAIMS

What is claimed is:

1. An isolated compound having the structure:



(I)

or pharmaceutically acceptable derivative thereof;

wherein **R′** is hydrogen or an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R', taken together with R^2 or a substituent present on R^1, may form a cycloheteroaliphatic moiety;

R^1 is an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^1, taken together with R′, may form a cycloheteroaliphatic moiety;

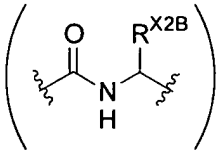
X^1 is –C(=O)-, -S(=O)-, -C(=NH)-, -C(=S)-, -NC(=O)-, -NC(=S)-, -N-C(=N-C≡N)-, -$NS(O_2)$-, -CHR^{X1A}-, -SO_2-, -COO-, -$C(=O)C(R^{X1A})_2$-, or -SC(=O)- wherein each occurrence of R^{X1A} is independently hydrogen, or an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

R^2 is an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^2, taken together with R', may form a cycloheteroaliphatic moiety;

R^3 is hydrogen, halogen, or an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

$R^{3'}$ is hydrogen, halogen, or lower alkyl;

R^4 is hydrogen, an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^4, taken together with a substituent present on X^2 or X^3, may form a cycloaliphatic, cycloheteroaliphatic, aromatic, or heteroaromatic moiety;

X^2 is absent, -NR^{X2A}-, -$(CHR^{X2A})_j$-, -$NR^{X2A}Y$-, -$(CHR^{X2A})_jY$- or -$N(R^{X2A})CH(R^{X2A'})Y$- wherein each occurrence of R^{X2A} is independently hydrogen or an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety; each occurrence of Y is independently  wherein, for each independent occurrence of t, R^{X2B} is hydrogen, or an aliphatic, heteroaliphatic,

aromatic or heteroaromatic moiety, or R^{X2A} or one occurrence of R^{X2B} taken together with R^4 may form a cycloaliphatic, cycloheteroaliphatic, aromatic or heteroaromatic moiety, and wherein each occurrence of j and t is independently an integer from 1 to 4; and

$\mathbf{X^3}$ is absent, -NHCO-, $-NHSO_2-$, -NHCONH-, -NHCOO-, $-CH_2NH-$, –C(=O)-, -S(=O)-, -C(=NH)-, -C(=S)-, -NC(=S)N-, -N-C(=N-C≡N)N-, $-NS(O_2)N-$, $-SO_2-$, $-C(=O)NR^{X3A}-$, $-C(=S)NR^{X3A}-$, -COO-, $-(CHR^{X3A})_k-$, -O-, $-CH_2NR^{X3A}-$, or $-NR^{X3A}-$, wherein each occurrence of R^{X3A} is independently hydrogen, an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^{X3A} taken together with R^4 may form a cycloaliphatic, cycloheteroaliphatic, aromatic or heteroaromatic moiety, and k is an integer from 1 to 3.

2. The compound of claim 1 wherein one or more of the following groups do not occur simultaneously as defined:

(i) $\mathbf{R'}$, $\mathbf{R^3}$ and $\mathbf{R^{3'}}$ are each hydrogen; $\mathbf{R^2}$ is alkyl, cycloalkylalkyl or aralkyl; $\mathbf{-X^2-X^3-R^4}$ together represents $-CHR^eC(=O)NHCH(R^w)C(=O)NR^xR^y$, wherein R^e is hydrogen or alkyl, R^w is alkyl, and one of R^x or R^y represents hydrogen and the other represents hydrogen, alkyl, aryl, aralkyl, 1-alkoxycarbonyl-2-phenylethyl, 1-alkoxycarbonyl-2-(imidazol-4-yl)ethyl, 2-(imidazol-1-yl)ethyl, indanyl, heterocyclyl-alkyl, carboxyalkyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl, aralkoxycarbonylalkyl or a group of the formula $-A-N(R^a)(R^b)$ in which A represents alkylene and R^a and R^b each represents alkyl or R^a and R^b together represent a pentamethylene group in which one methylene group can be replaced by NH, N-alkyl, N-alkanoyl, N-aralkoxycarbonyl, O, S, SO, or SO_2; or R^x and R^y together with the nitrogen atom to which they are attached represent a 1,2,3,4-tetrahydroisoquinoline ring; and $\mathbf{-X^1-R^1}$ together represents an alkoxycarbonyl, aralkoxycarbonyl, alkanoyl, aralkanoyl, aroyl, cycloalkylcarbonyl, heterocyclylcarbonyl, heterocyclyl-alkanoyl, 6-(dibenzylcarbamoyl)-4-oxohexanoyl moiety or an acyl group of an α-amino acid in which the amino group is substituted by an alkoxycarbonyl, aralkoxycarbonyl, diaralkylcarbamoyl, diaralkylalkanoyl, or aralkanoyl moiety;

wherein the term "aroyl" refers to an acyl group derived from from an arylcarboxylic acid such as benzoyl, 1-naphthoyl, 2-naphthoyl, etc., and the term "aralkanoyl" refers to an acyl group derived from an aryl-substituted alkanecarboxylic acid;

whereby the term "aryl" alone or in each of the aralkyl, aryloxycarbonylalkyl, aralkoxycarbonylalkyl or N-aralkoxycarbonyl moieties refers to a phenyl or naphthyl group

optionally substituted with one or emore substituents selected from alkyl, hydroxy, alkoxy and halogen;

(ii) **R′**, **R³** and **R³′** are each hydrogen; **X¹** is -C(=O)-, -SO_2-, $N(R^x)SO_2$, $N(R^x)C(=O)$ or $SC(=O)$, wherein R^x is hydrogen, C_{1-5}alkyl or joined together with R^1 either directly to form a 5-7 membered heterocycle such as pyrrolidinyl or piperidinyl, or through a heteroatom selected from N, O and S, to form a 6-membered heterocycle with the nitrogen to which they are attached such as morpholinyl, piperazyl, or N-C_{1-3}alkyl-piperazyl; **R¹** is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, $N(R^a)_2$, $C(=O)OR^a$, $-C(=O)N(R^a)_2$, $-SO_2N(R^a)_2$, $CH_2N(R^a)_2$, $N(R^a)C(=O)R^a$ or $N(R^a)SO_2R^a$; **R²** is OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; and **$-X^2$-X^3-R^4** together represent $-CH(R^d)C(=O)NHCH(R^e)C(=O)$-Y-$[CR^fR^g]_mR^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d and R^e are independently hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$ wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring;

(iii) **R′**, **R³** and **R³′** are each hydrogen; **X¹** is -C(=O)-, -SO_2-, $N(R^x)SO_2$, $N(R^x)C(=O)$ or $SC(=O)$, wherein R^x is hydrogen, C_{1-5}alkyl or joined together with R^1 either directly to form a 5-7 membered heterocycle such as pyrrolidinyl or piperidinyl, or through a heteroatom selected from N, O and S, to form a 6-membered heterocycle with the nitrogen to which they are attached such as morpholinyl, piperazyl, or N-C_{1-3}alkyl-piperazyl; **R¹** is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, $N(R^a)_2$, $C(=O)OR^a$, $-C(=O)N(R^a)_2$, $-SO_2N(R^a)_2$, $CH_2N(R^a)_2$, $N(R^a)C(=O)R^a$ or $N(R^a)SO_2R^a$; **R²** is OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; and **$-X^2$-X^3-R^4** together represent $-CH(R^d)C(=O)$-Y-$[CR^fR^g]_mR^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d is hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is

hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring;

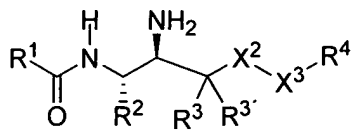
(iv) $\mathbf{R'}$ and $\mathbf{R^{3'}}$ are each hydrogen; $\mathbf{X^1}$ is -C(=O)-, -SO_2-, $N(R^x)SO_2$, $N(R^x)C(=O)$ or SC(=O), wherein R^x is hydrogen, C_{1-5}alkyl or joined together with R^1 either directly to form a 5-7 membered heterocycle such as pyrrolidinyl or piperidinyl, or through a heteroatom selected from N, O and S, to form a 6-membered heterocycle with the nitrogen to which they are attached such as morpholinyl, piperazyl, or N-C_{1-3}alkyl-piperazyl; $\mathbf{R^1}$ is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, $N(R^a)_2$, $C(=O)OR^a$, $-C(=O)N(R^a)_2$, $-SO_2N(R^a)_2$, $CH_2N(R^a)_2$, $N(R^a)C(=O)R^a$ or $N(R^a)SO_2R^a$; $\mathbf{R^2}$ is OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; $\mathbf{R^3}$ is hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; and $\mathbf{-X^2-X^3-R^4}$ together represent $-CH(R^d)C(=O)NHCH(R^e)C(=O)$-Y-$[CR^fR^g]_mR^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d and R^e are independently hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$ wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring;

(v) $\mathbf{R'}$ and $\mathbf{R^{3'}}$ are each hydrogen; $\mathbf{X^1}$ is -C(=O)-, -SO_2-, $N(R^x)SO_2$, $N(R^x)C(=O)$ or SC(=O), wherein R^x is hydrogen, C_{1-5}alkyl or joined together with R^1 either directly to form a 5-7 membered heterocycle such as pyrrolidinyl or piperidinyl, or through a heteroatom selected from N, O and S, to form a 6-membered heterocycle with the nitrogen to which they are attached such as morpholinyl, piperazyl, or N-C_{1-3}alkyl-piperazyl; $\mathbf{R^1}$ is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, $N(R^a)_2$, $C(=O)OR^a$, $-C(=O)N(R^a)_2$, $-SO_2N(R^a)_2$,

$CH_2N(R^a)_2$, $N(R^a)C(=O)R^a$ or $N(R^a)SO_2R^a$; $\mathbf{R^2}$ is OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; $\mathbf{R^3}$ is hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; and $\mathbf{-X^2-X^3-R^4}$ together represent $-CH(R^d)C(=O)$-Y-$[CR^fR^g]_mR^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d is hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring; and

(vi) $\mathbf{R'}$, $\mathbf{R^3}$ and $\mathbf{R^{3'}}$ are each hydrogen; $\mathbf{R^2}$ is C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl, T-C_{2-6}alkenyl, wherein T is aryl, heteroaryl or C_{3-7}cycloalkyl; $\mathbf{R^1-X^1}$ together represent W wherein W is R^x, R^xCO, R^xOCO, $R^xOCH(R^y)CO$, $R^xNHCH(R^y)CO$, $R^xSCH(R^y)CO$, R^xSO_2, R^xSO or an amino acid with a blocked or unblocked amino terminus, wherein R^x and R^y are each independently hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl or T-$(CH_2)_nCH(T)(CH_2)_n$ wherein n is an integer from 1 to 4; and $\mathbf{-X^2-X^3-R^4}$ together represent $-CH(R^a)C(=X)CHR^bR^c$, wherein X is (OH,H) or O; R^a is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl or T-C_{2-6}alkenyl; R^b is hydrogen or OH; and R^c is Y, $(CHR^w)_n$-Y or $=CR^z(CHR^w)_n$-Y, wherein Y is hydrogen, OH, $-NR^wR^q$, aryl, heteroaryl or CO-Z, n is an integer from 1 to 4, Z is OH, $-NR^wR^q$, OR^w or an amino acid with a blocked or unblocked carboxy terminus, R^q is H, C_{1-6}alkyl or arylC_{1-6}alykl, and R^z and R^w are each independently hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl or T-C_{2-6}alkenyl.

3. The compound of claim 1 having the structure:



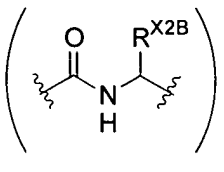
or pharmaceutically acceptable derivative thereof;

wherein $\mathbf{R^1}$ is an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

$\mathbf{R^2}$ is an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^2, taken together with R', may form a cycloheteroaliphatic moiety;

$\mathbf{R^3}$ is hydrogen, halogen, or an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety;

$\mathbf{R^4}$ is hydrogen, an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^4, taken together with a substituent present on X^2 or X^3, may form a cycloaliphatic, cycloheteroaliphatic, aromatic, or heteroaromatic moiety;

$\mathbf{X^2}$ is absent, $-NR^{X2A}-$, $-(CHR^{X2A})_j-$, $-NR^{X2A}Y-$, $-(CHR^{X2A})_jY-$ or $-N(R^{X2A})CH(R^{X2A'})Y-$ wherein each occurrence of R^{X2A} is independently hydrogen or an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety; each occurrence of Y is independently 

t wherein, for each independent occurrence of t, R^{X2B} is hydrogen, or an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^{X2A} or one occurrence of R^{X2B} taken together with R^4 may form a cycloaliphatic, cycloheteroaliphatic, aromatic or heteroaromatic moiety, and wherein each occurrence of j and t is independently an integer from 1 to 4; and

$\mathbf{X^3}$ is absent, $-NHCO-$, $-NHSO_2-$, $-NHCONH-$, $-NHCOO-$, $-CH_2NH-$, $-C(=O)-$, $-S(=O)-$, $-C(=NH)-$, $-C(=S)-$, $-NC(=S)N-$, $-N-C(=N-C\equiv N)N-$, $-NS(O_2)N-$, $-SO_2-$, $-C(=O)NR^{X3A}-$, $-C(=S)NR^{X3A}-$, $-COO-$, $-(CHR^{X3A})_k-$, $-O-$, $-CH_2NR^{X3A}-$, or $-NR^{X3A}-$, wherein each occurrence of R^{X3A} is independently hydrogen, an aliphatic, heteroaliphatic, aromatic or heteroaromatic moiety, or R^{X3A} taken together with R^4 may form a cycloaliphatic, cycloheteroaliphatic, aromatic or heteroaromatic moiety, and k is an integer from 1 to 3.

4. The compound of claim 3 wherein one or more of the following groups do not occur simultaneously as defined:

(i) $\mathbf{R^3}$ and $\mathbf{R^{3'}}$ are each hydrogen; $\mathbf{R^2}$ is alkyl, cycloalkylalkyl or aralkyl; $\mathbf{-X^2-X^3-R^4}$ together represents $-CHR^eC(=O)NHCH(R^w)C(=O)NR^xR^y$, wherein R^e is hydrogen or alkyl, R^w is alkyl, and one of R^x or R^y represents hydrogen and the other represents hydrogen, alkyl, aryl, aralkyl, 1-alkoxycarbonyl-2-phenylethyl, 1-alkoxycarbonyl-2-(imidazol-4-yl)ethyl, 2-(imidazol-1-yl)ethyl, indanyl, heterocyclyl-alkyl, carboxyalkyl, alkoxycarbonylalkyl, aryloxycarbonylalkyl,

aralkoxycarbonylalkyl or a group of the formula –A-N(R^a)(R^b) in which A represents alkylene and R^a and R^b each represents alkyl or R^a and R^b together represent a pentamethylene group in which one methylene group can be replaced by NH, N-alkyl, N-alkanoyl, N-aralkoxycarbonyl, O, S, SO, or SO_2; or R^x and R^y together with the nitrogen atom to which they are attached represent a 1,2,3,4-tetrahydroisoquinoline ring; and **–C(=O)-R^1** together represents an alkoxycarbonyl, aralkoxycarbonyl, alkanoyl, aralkanoyl, aroyl, cycloalkylcarbonyl, heterocyclylcarbonyl, heterocyclyl-alkanoyl, 6-(dibenzylcarbamoyl)-4-oxohexanoyl moiety or an acyl group of an α-amino acid in which the amino group is substituted by an alkoxycarbonyl, aralkoxycarbonyl, diaralkylcarbamoyl, diaralkylalkanoyl, or aralkanoyl moiety;

wherein the term "aroyl" refers to an acyl group derived from from an arylcarboxylic acid such as benzoyl, 1-naphthoyl, 2-naphthoyl, etc., and the term "aralkanoyl" refers to an acyl group derived from an aryl-substituted alkanecarboxylic acid;

whereby the term "aryl" alone or in each of the aralkyl, aryloxycarbonylalkyl, aralkoxycarbonylalkyl or N-aralkoxycarbonyl moieties refers to a phenyl or naphthyl group optionally substituted with one or emore substituents selected from alkyl, hydroxy, alkoxy and halogen;

(ii) **R^3** and **$R^{3'}$** are each hydrogen; **R^1** is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, N(R^a)$_2$, C(=O)OR^a, –C(=O)N(R^a)$_2$, –SO_2N(R^a)$_2$, CH_2N(R^a)$_2$, N(R^a)C(=O)R^a or N(R^a)SO_2R^a; **R^2** is OR^a, N(R^a)$_2$, C_{1-4}alkenyl-R^c or –[CR^bR^c]$_n$$R^c$; and **–$X^2$-$X^3$-$R^4$** together represent –CH(R^d)C(=O)NHCH(R^e)C(=O)-Y-[CR^fR^g]$_m$$R^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d and R^e are independently hydrogen, OR^a, N(R^a)$_2$, C_{1-4}alkenyl-R^c or –[CR^bR^c]$_n$$R^c$ wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring;

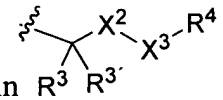
(iii) $\mathbf{R^3}$ and $\mathbf{R^{3'}}$ are each hydrogen; $\mathbf{R^1}$ is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, $N(R^a)_2$, $C(=O)OR^a$, $-C(=O)N(R^a)_2$, $-SO_2N(R^a)_2$, $CH_2N(R^a)_2$, $N(R^a)C(=O)R^a$ or $N(R^a)SO_2R^a$; $\mathbf{R^2}$ is OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; and $\mathbf{-X^2-X^3-R^4}$ together represent $-CH(R^d)C(=O)$-Y-$[CR^fR^g]_mR^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d is hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring;

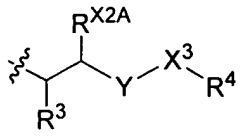
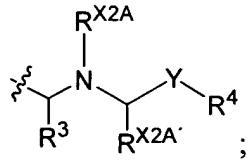
(iv) $\mathbf{R^{3'}}$ is hydrogen; $\mathbf{R^1}$ is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, $N(R^a)_2$, $C(=O)OR^a$, $-C(=O)N(R^a)_2$, $-SO_2N(R^a)_2$, $CH_2N(R^a)_2$, $N(R^a)C(=O)R^a$ or $N(R^a)SO_2R^a$; $\mathbf{R^2}$ is OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; $\mathbf{R^3}$ is hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; and $\mathbf{-X^2-X^3-R^4}$ together represent $-CH(R^d)C(=O)NHCH(R^e)C(=O)$-Y-$[CR^fR^g]_mR^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d and R^e are independently hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$ wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring;

(v) $\mathbf{R^{3'}}$ is hydrogen; $\mathbf{R^1}$ is a substituted or unsubstituted C_{1-6}alkyl, a 5-6 membered heterocycle or a 6-10 carbon atoms aryl moiety substituted with C_{1-4}alkyl, C_{1-3}alkoxy, hydroxy, halogen, $N(R^a)_2$, $C(=O)OR^a$, $-C(=O)N(R^a)_2$, $-SO_2N(R^a)_2$, $CH_2N(R^a)_2$, $N(R^a)C(=O)R^a$ or $N(R^a)SO_2R^a$; $\mathbf{R^2}$ is OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; $\mathbf{R^3}$ is hydrogen, OR^a, $N(R^a)_2$, C_{1-}

$_4$alkenyl-R^c or $-[CR^bR^c]_nR^c$; and $\mathbf{-X^2-X^3-R^4}$ together represent $-CH(R^d)C(=O)-Y-[CR^fR^g]_mR^g$, wherein m is an integer from 0 to 5, Y is O or NH, R^d is hydrogen, OR^a, $N(R^a)_2$, C_{1-4}alkenyl-R^c or $-[CR^bR^c]_nR^c$; wherein n is an integer from 0 to 5, R^a is hydrogen or C_{1-4}alkyl, R^b is hydrogen, hydroxy or C_{1-4}alkyl and R^c is hydrogen, substituted or unsubstituted aryl, 5- or 6-membered heterocycle, C_{1-6}alkyl or C_{1-6}alkenyl, C_{3-7}cycloalkyl, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring, benzofuryl, indolyl, azabicyclo C_{7-11}cycloalkyl or benzopiperidinyl; R^f is hydrogen, substituted or unsubstituted C_{1-6}alkyl or $(CH_2CH_2O)_pCH_3$ or $(CH_2CH_2O)_pH$ wherein p is an integer from 0 to 5, and R^g is hydrogen, or substituted or unsubstituted aryl, heterocycle, 5- to 7-membered carbocyclic or 7- to 10-membered bicyclic carbocyclic ring; and

(vi) $\mathbf{R^3}$ and $\mathbf{R^{3'}}$ are each hydrogen; $\mathbf{R^2}$ is C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl, T-C_{2-6}alkenyl, wherein T is aryl, heteroaryl or C_{3-7}cycloalkyl; $\mathbf{R^1-C(=O)-}$ together represent W wherein W is R^x, R^xCO, R^xOCO, $R^xOCH(R^y)CO$, $R^xNHCH(R^y)CO$, $R^xSCH(R^y)CO$, R^xSO_2, R^xSO or an amino acid with a blocked or unblocked amino terminus, wherein R^x and R^y are each independently hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl or T-$(CH_2)_nCH(T)(CH_2)_n$ wherein n is an integer from 1 to 4; and $\mathbf{-X^2-X^3-R^4}$ together represent $-CH(R^a)C(=X)CHR^bR^c$, wherein X is (OH,H) or O; R^a is hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl or T-C_{2-6}alkenyl; R^b is hydrogen or OH; and R^c is Y, $(CHR^w)_n$-Y or $=CR^z(CHR^w)_n$-Y, wherein Y is hydrogen, OH, $-NR^wR^q$, aryl, heteroaryl or CO-Z, n is an integer from 1 to 4, Z is OH, $-NR^wR^q$, OR^w or an amino acid with a blocked or unblocked carboxy terminus, R^q is H, C_{1-6}alkyl or arylC_{1-6}alykl, and R^z and R^w are each independently hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl, aryl, heteroaryl, T-C_{1-6}alkyl or T-C_{2-6}alkenyl.

5. The compound of claim 3, wherein  has one of the following structures:

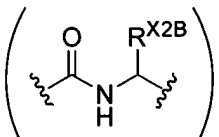
 or  ;

wherein $\mathbf{R^3}$ is hydrogen, halogen or an aliphatic, heteroaliphatic, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, or –(heteroalkyl)heteroaryl moiety;

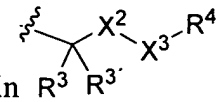
$\mathbf{R^4}$ is an aliphatic, heteroaliphatic, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, or –(heteroalkyl)heteroaryl moiety, or R^4, taken together with $R^{X2A'}$ or a substituent present on Y or X^3, may form a cycloaliphatic, cycloheteroaliphatic, aryl, or heteroaryl moiety;

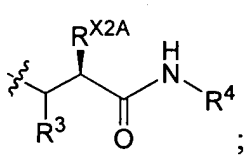
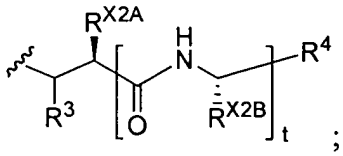
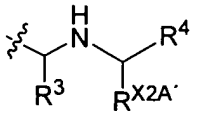
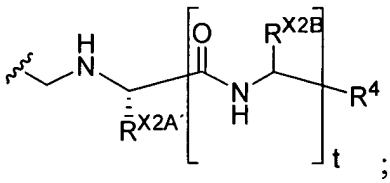
$\mathbf{R^{X2A}}$ is hydrogen or an aliphatic, heteroaliphatic, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, or –(heteroalkyl)heteroaryl moiety;

$\mathbf{R^{X2A'}}$ is hydrogen, or an aliphatic, heteroaliphatic, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, or –(heteroalkyl)heteroaryl moiety, or $R^{X2A'}$ taken together with R^4 may form a cycloaliphatic, cycloheteroaliphatic, aryl or heteroaryl moiety;

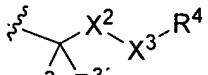
Y is independently absent or is  , wherein, for each independent occurrence of t, R^{X2B} is hydrogen, or an aliphatic, heteroaliphatic, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, or –(heteroalkyl)heteroaryl moiety, or one occurrence of R^{X2B} taken together with R^4 may form a cycloaliphatic, cycloheteroaliphatic, aryl or heteroaryl moiety; t is an integer from 1 to 4; and

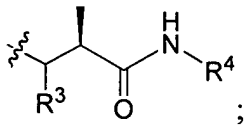
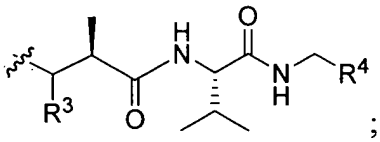
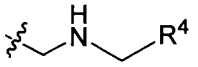
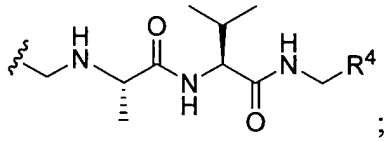
$\mathbf{X^3}$ is absent, -NHCO-, $-NHSO_2-$, -NHCONH-, -NHCOO-, $-CH_2NH-$, –C(=O)-, -S(=O)-, -C(=NH)-, -C(=S)-, -NC(=S)N-, -N-C(=N-C≡N)N-, $-NS(O_2)N-$, $-SO_2-$, $-C(=O)NR^{X3A}-$, $-C(=S)NR^{X3A}-$, -COO-, $(CHR^{X3A})_k$, -O-, $-CH_2NR^{X3A}-$, or $-NR^{X3A}-$, wherein each occurrence of R^{X3A} is independently hydrogen, an aliphatic, heteroaliphatic, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, or –(heteroalkyl)heteroaryl moiety, or R^{X3A} taken together with R^4 may form a cycloaliphatic, cycloheteroaliphatic, aryl or heteroaryl moiety, and k is an integer from 1 to 3.

6. The compound of claim 5, wherein  has one of the following structures:


;

;

or

;

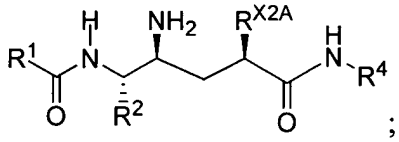
wherein R^3, R^4, R^{X2A}, $R^{X2A'}$, R^{X2B} and t are as defined in claim 2.

7. The compound of claim 5, wherein  has one of the following structures:


;

;

or

;

wherein R^3 and R^4 are as defined in claim 2.

8. The compound of claim 3 having the structure:

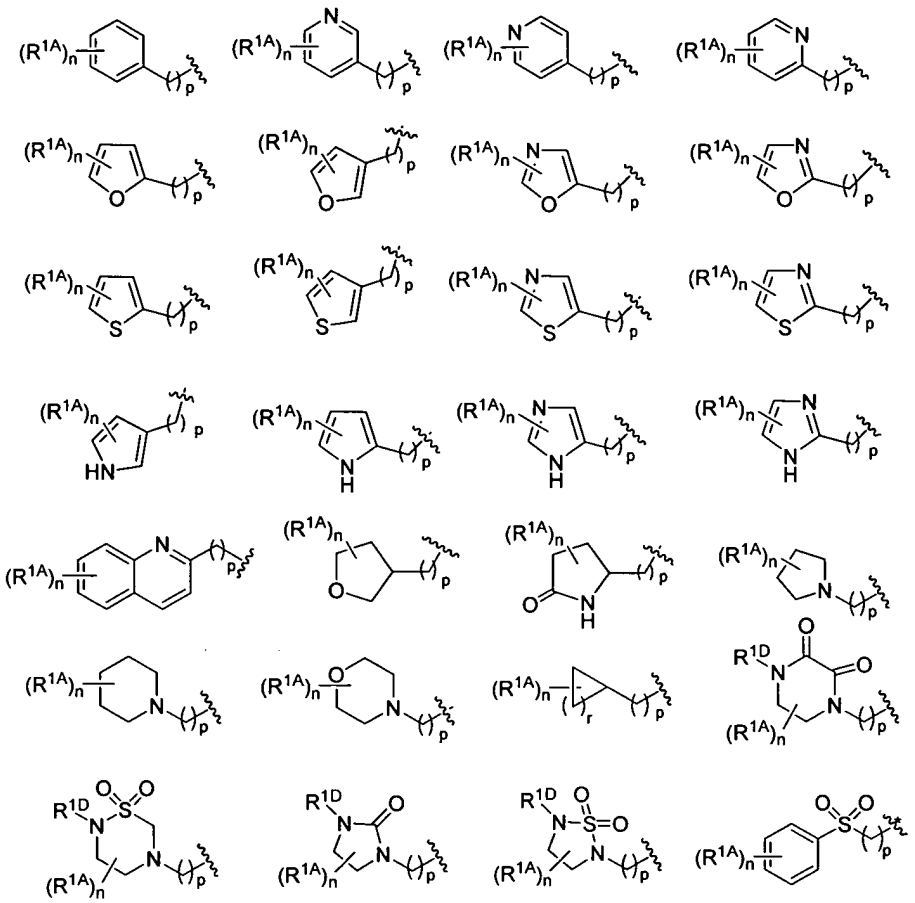

;

wherein R^{X2A} is hydrogen or an aliphatic, heteroaliphatic, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, or –(heteroalkyl)heteroaryl moiety.

9. The compound of claim 8, wherein R^{X2A} is a substituted or unsubstituted, linear or branched lower alkyl moiety.

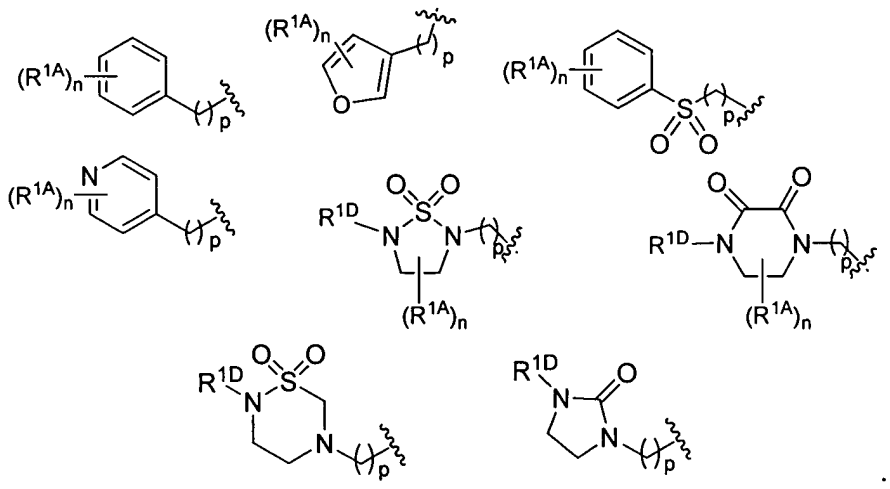
10. The compound of claim 5, wherein R^{X2A} is methyl, ethyl, propyl, isopropyl or phenethyl.

11. The compound of claim 3 or 8, wherein R^1 has one of the following structures:

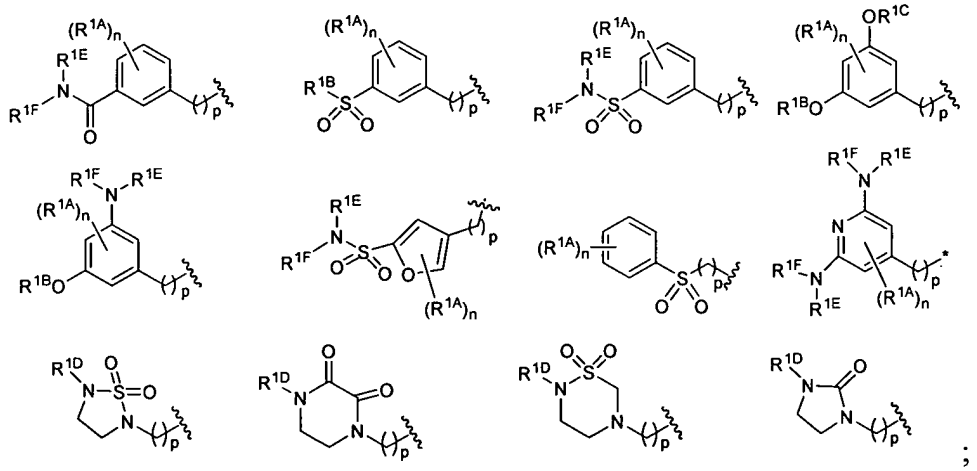


wherein R^{1A} is hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, $-OR^{1B}$, $-SR^{1B}$, $-N(R^{1B})_2$, $-SO_2N(R^{1B})_2$, $-C(=O)N(R^{1B})_2$, halogen, -CN, $-NO_2$, $-C(=O)OR^{1B}$, $N(R^{1B})C(=O)R^{1C}$ or $-N(R^{1B})SO_2R^{1C}$; wherein each occcurrence of R^{1B} and R^{1C} is independently hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl; or R^{1B} and R^{1C}, taken together with the atoms to which they are attached, form a substituted or unsubstituted heterocyclic moiety; R^{1D} is hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, acyl or a nitrogen protecting group; wherein n and p are each independently integers from 0 to 3 and r is an integer from 1 to 6; whereby each of the foregoing alkyl and heteroalkyl moieties may be linear or branched, substituted or unsubstituted, cyclic or acylic, and each of the foregoing aryl, heteroaryl, -(alkyl)aryl and -(alkyl)heteroaryl moieties may be substituted or unsusbtituted.

12. The compound of claim 11, wherein R^1 has one of the following structures:



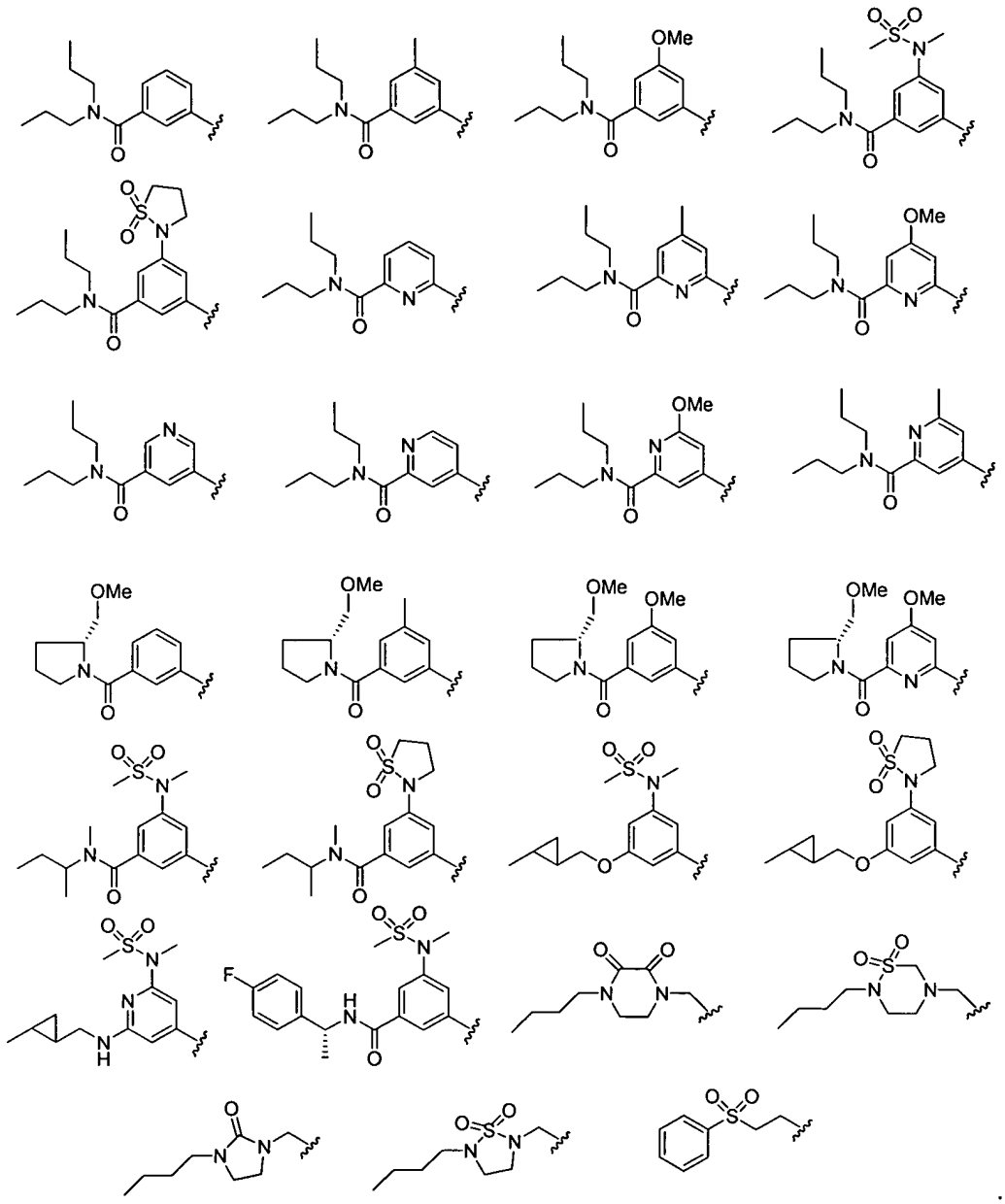
13. The compound of claim 11, wherein R^1 has one of the following structures:



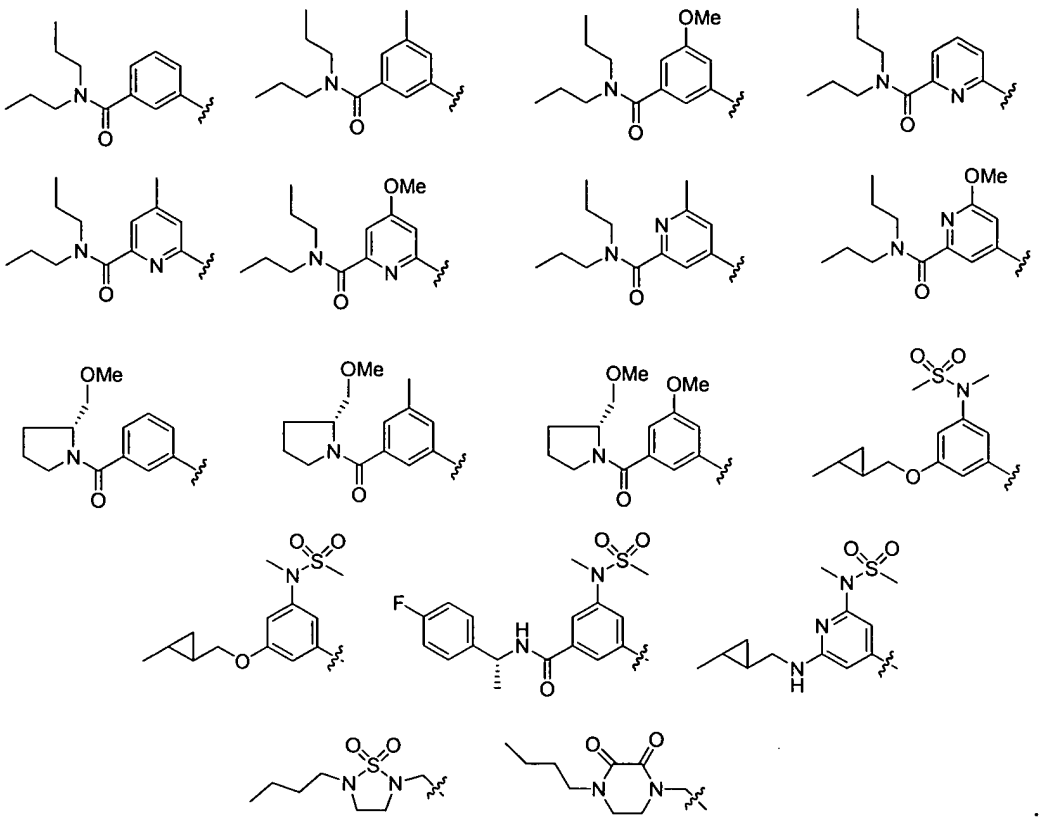
;

wherein R^{1D} is hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl; -(alkyl)heteroaryl or acyl; R^{1E} and R^{1F} are each independently hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, $-C(=O)R^{1C}$ or $-SO_2R^{1C}$, where R^{1C} is hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl; or R^{1E} and R^{1F} taken together form a 5-8 membered heterocyclic ring; or R^{1E} and one occurrence of R^{1A}, taken together, form a substituted or unsubstituted, saturated or unsaturated heterocyclic ring.

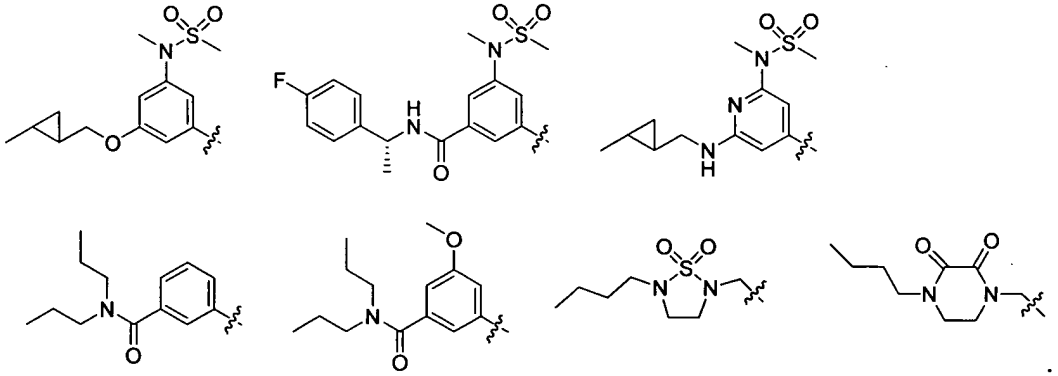
14. The compound of claim 11, wherein R^1 has one of the following structures:



15. The compound of claim 11, wherein R^1 has one of the following structures:



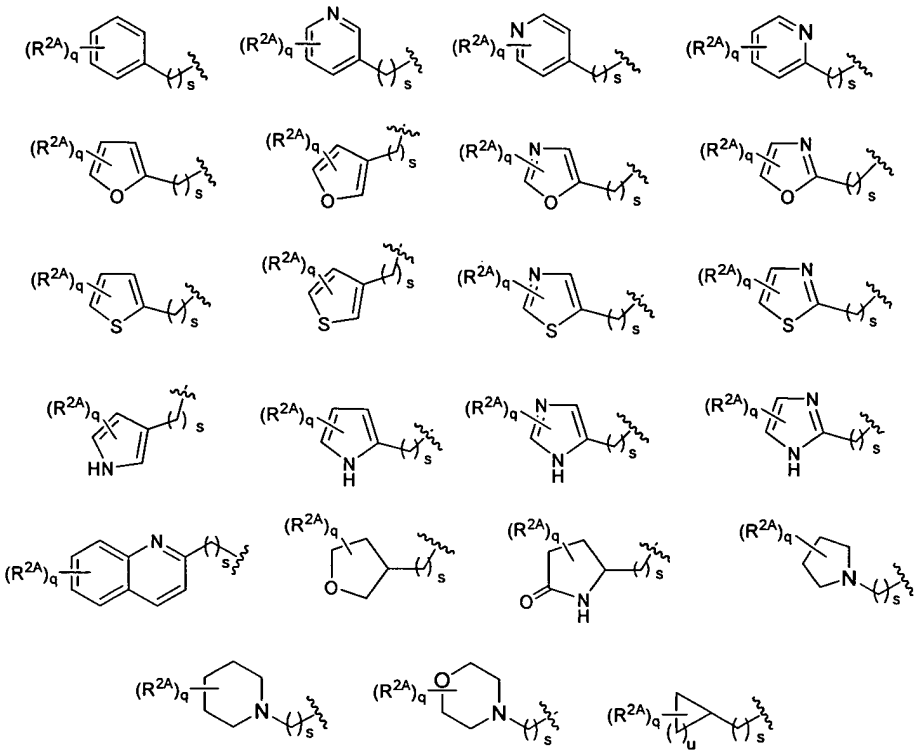
16. The compound of claim 11, wherein R^1 has one of the following structures:



17. The compound of claim 3 or 8, wherein R^2 is lower alkyl, $-CH_2NR^{2A}R^{2B}$ or $-(CH_2)$phenyl, wherein the phenyl group is optionally substituted with one or more occurrences of R^{2C}, wherein R^{2C} is hydrogen, alkyl, alkoxy or halogen; and wherein R^{2A} and R^{2B} are each independently hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl; whereby each of the foregoing alkyl and heteroalkyl moieties may be linear or

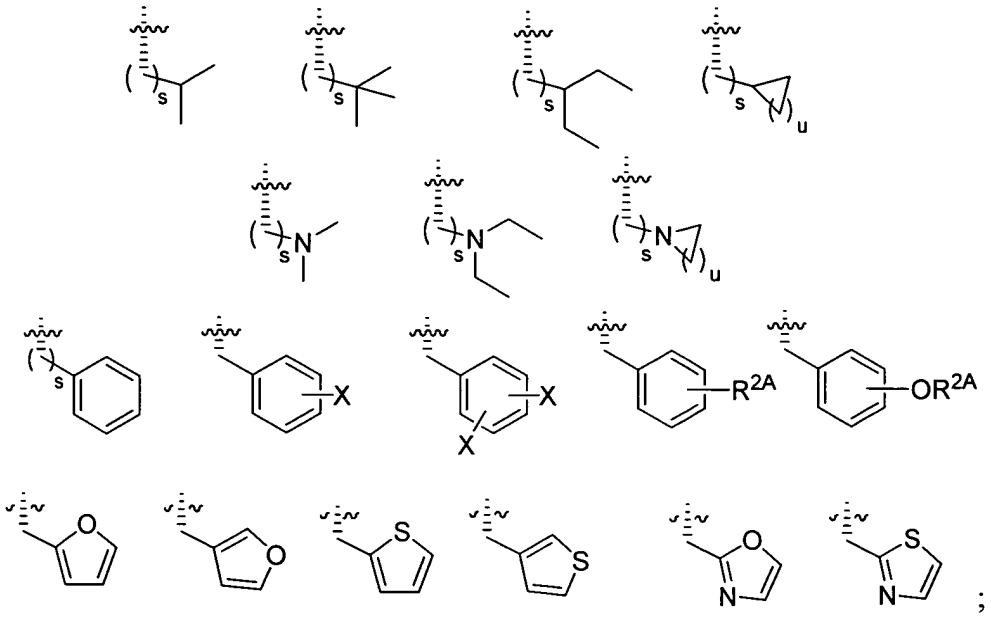
branched, substituted or unsubstituted, cyclic or acylic, and each of the foregoing aryl, heteroaryl, -(alkyl)aryl and -(alkyl)heteroaryl moieties may be substituted or unsusbtituted.

18. The compound of claim 17, wherein R^2 has one of the following structures:



wherein R^{2A} is hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl, $-OR^{2B}$, $-SR^{2B}$, $-N(R^{2B})_2$, $-SO_2N(R^{2B})_2$, $-C(=O)N(R^{2B})_2$, halogen, -CN, $-NO_2$, $-C(=O)OR^{2B}$, $-N(R^{2B})C(=O)R^{2C}$, wherein each occcurrence of R^{2B} and R^{2C} is independently hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl, wherein q and s are each independently integers from 0 to 3 and u is an integer from 1 to 6; whereby each of the foregoing alkyl and heteroalkyl moieties may be linear or branched, substituted or unsubstituted, cyclic or acylic, and each of the foregoing aryl, heteroaryl, -(alkyl)aryl and -(alkyl)heteroaryl moieties may be substituted or unsusbtituted.

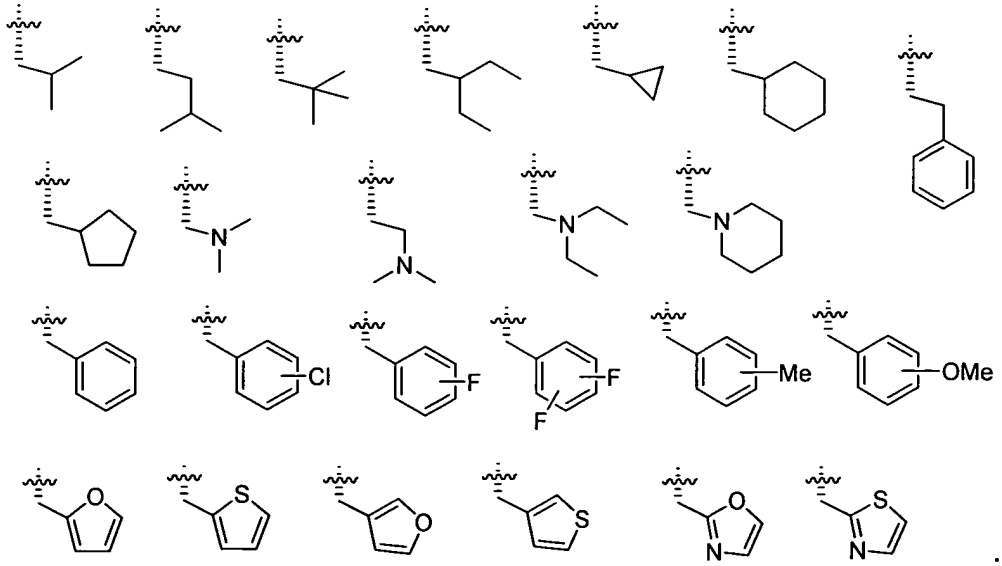
19. The compound of claim 17, wherein R^2 has one of the following structures:



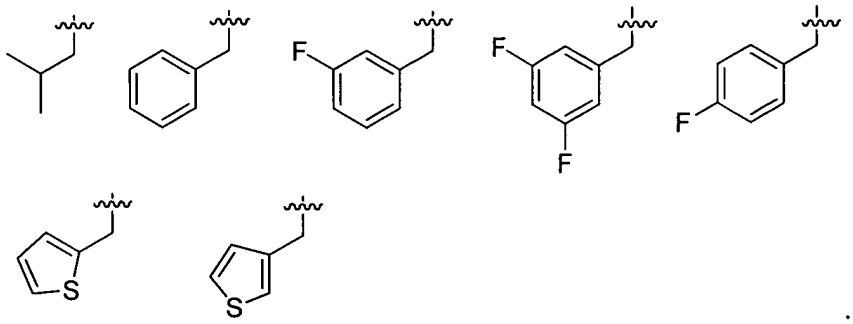
wherein each occcurrence of R^{2A} is independently hydrogen or lower alkyl; each occurrence of X is independently a halogen; s is an integer from 0 to 3 and u is an integer from 1 to 6; whereby each of the foregoing alkyl moieties may be linear or branched, substituted or unsubstituted and cyclic or acylic.

20. The compound of claim 17, wherein each occurrence of X is independenly chlorine or fluorine and R^{2A} is methyl.

21. The compound of claim 17, wherein R^2 has one of the following structures:



22. The compound of claim 17, wherein R^2 has one of the following structures:

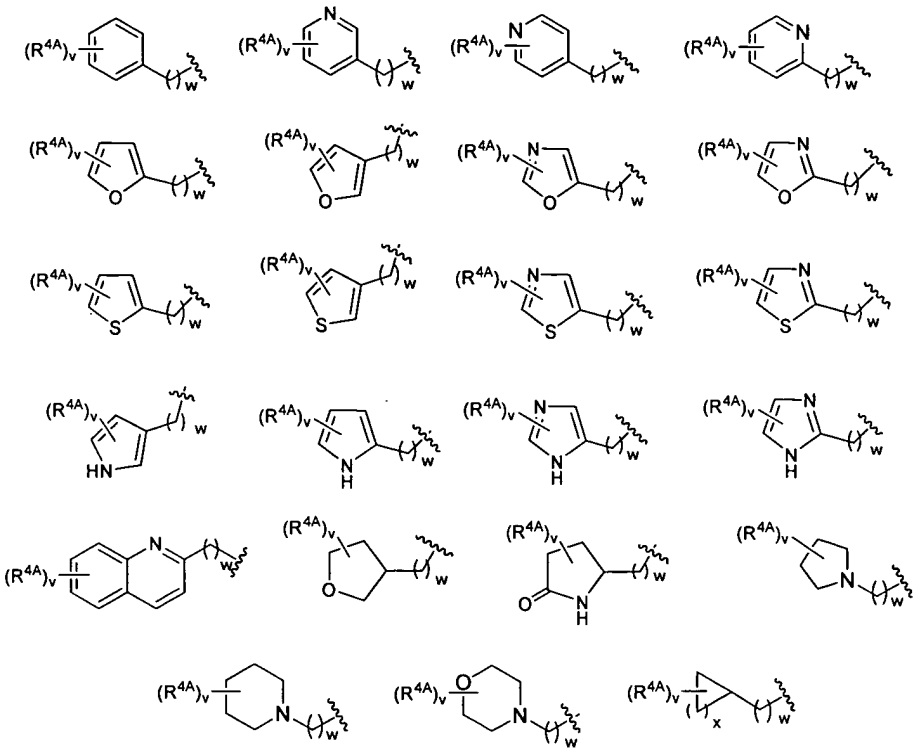


23. The compound of claim 3, wherein R^3 is hydrogen or halogen.

24. The compound of claim 3 or 8, wherein R^4 is substituted or unsubstituted, linear or branched, cyclic or acyclic alkyl, phenyl or $-(CH_2)$phenyl, wherein the phenyl group is optionally substituted with one or more occurrences of R^{4A}, wherein R^{4A} is hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl, $-OR^{4B}$, $-SR^{4B}$, $-N(R^{4B})_2$, $-SO_2N(R^{4B})_2$, $-C(=O)N(R^{4B})_2$, halogen, -CN, $-NO_2$, $-C(=O)OR^{4B}$, $-N(R^{4B})C(=O)R^{4C}$, wherein each occcurrence of R^{4B} and R^{4C} is independently hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl, -(heteroalkyl)heteroaryl.

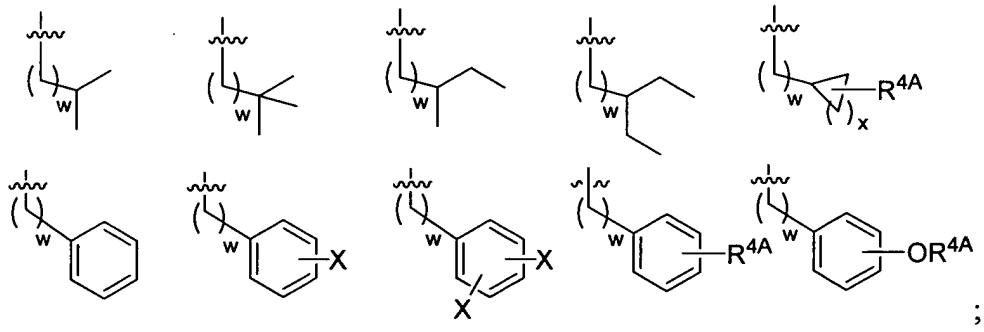
25. The compound of claim 24, wherein R^4 is substituted or unsubstituted, linear or branched, cyclic or acyclic alkyl, phenyl or $-(CH_2)$phenyl, wherein the phenyl group is optionally substituted with one or more occurrences of R^{4A}, wherein R^{4A} is hydrogen, hydroxyl, alkyl, alkoxy or halogen.

26. The compound of claim 24, wherein R^4 has one of the following structures:



wherein each occurrence of R^{4A} is independently hydrogen, alkyl, heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl, $-OR^{4B}$, $-SR^{4B}$, $-N(R^{4B})_2$, $-SO_2N(R^{4B})_2$, $-C(=O)N(R^{4B})_2$, halogen, -CN, $-NO_2$, $-C(=O)OR^{4B}$, $-N(R^{4B})C(=O)R^{4C}$, wherein each occcurrence of R^{4B} and R^{4C} is independently hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl, wherein v and w are each independently integers from 0 to 3 and x is an integer from 1 to 6; whereby each of the foregoing alkyl and heteroalkyl moieties may be linear or branched, substituted or unsubstituted, cyclic or acylic, and each of the foregoing aryl, heteroaryl, -(alkyl)aryl and -(alkyl)heteroaryl moieties may be substituted or unsusbtituted.

27. The compound of claim 24, wherein R^4 is methyl, ethyl, propyl or one of:

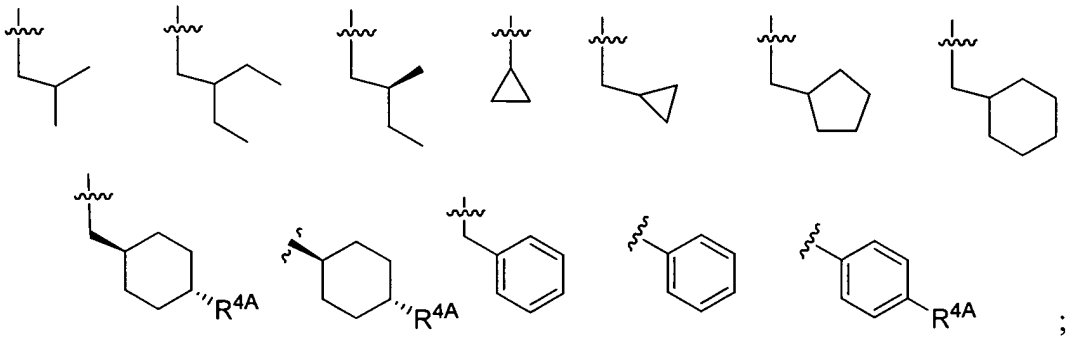


;

wherein each occcurrence of R^{4A} is independently hydrogen, lower alkyl or $C(=O)OR^{4B}$, wherein R^{4B} is hydrogen, lower alkyl, lower heteroalkyl, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl; each occurrence of X is independently a halogen; w is an integer from 0 to 3 and x is an integer from 1 to 6; whereby each of the foregoing alkyl and heteroalkyl moieties may be linear or branched, substituted or unsubstituted, cyclic or acylic, and each of the foregoing aryl, heteroaryl, -(alkyl)aryl and -(alkyl)heteroaryl moieties may be substituted or unsusbtituted.

28. The compound of claim 27, wherein each occurrence of X is independenly chlorine or fluorine and R^{4A} is methyl.

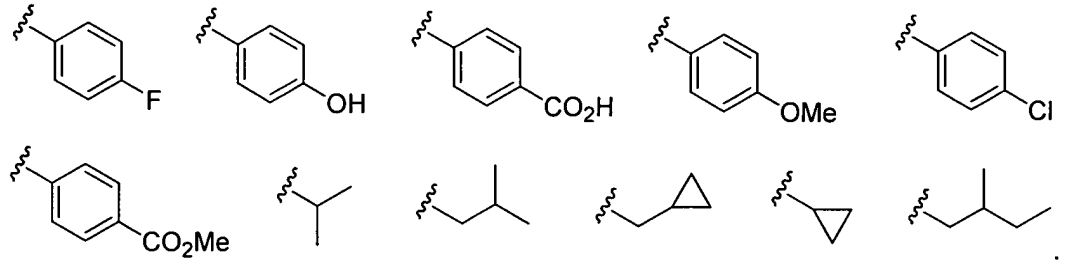
29. The compound of claim 24, wherein R^4 is methyl, ethyl, propyl or one of:



;

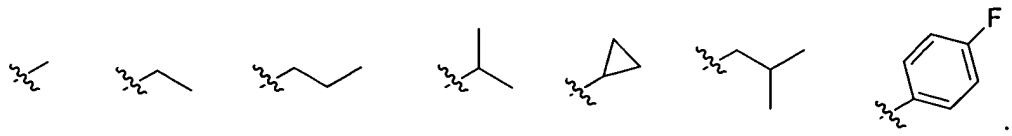
wherein R^{4A} is hydrogen, hydroxyl, lower alkyl, lower alkoxy, halogen, $C(=O)OR^{4B}$, aryl, heteroaryl, -(alkyl)aryl or -(alkyl)heteroaryl, wherein R^{4B} is hydrogen, lower alkyl, lower heteroalkyl, aryl, heteoraryl, -(alkyl)aryl, -(alkyl)heteroaryl, -(heteroalkyl)aryl or –(heteroalkyl)heteroaryl.

30. The compound of claim 24, wherein R^4 is methyl, ethyl, propyl, isopropyl or one of:



.

31. The compound of claim 24, wherein R^4 has one of the following structures:



32. A pharmaceutical composition comprising a compound of claim 3 or 8, and a pharmaceutically acceptable carrier or diluent, optionally further comprising an additional therapeutic agent.

33. The pharmaceutical composition of claim 32, wherein the compound is present in an amount effective to inhibit β-secretase activity.

34. The pharmaceutical composition of claim 32, wherein the additional therapeutic agent is an agent for the treatment of Alzheimer's Disease.

35. A method for inhibiting β-secretase activity in a patient or a biological sample, comprising administering to said patient, or contacting said biological sample with an effective inhibitory amount of a compound of claim 3 or 8.

36. A method for treating or preventing a disease characterized by β-amyloid deposits in the brain comprising administering to a patient a therapeutically effective amount of a compound of claim 3 or 8.

37. The method of claim 36, wherein the disease is Alzheimer's disease MCI (mild cognitive impairment), Down's syndrome, Hereditary Cerebral Hemmorhage with Amyloidosis of the Dutch-Type, cerebral amyloid angiopathy, other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, and diffuse Lewy body type Alzheimer's disease.